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## Health Policy Analysis

# Risk Attitudes and Personality Traits Predict Perceptions of Benefits and Risks for Medicinal Products: A Field Study of European Medical Assessors

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## ABSTRACT

**Background:** Risk attitudes and personality traits are known predictors of decision making among laypersons, but very little is known of their influence among experts participating in organizational decision making. **Methods:** Seventy-five European medical assessors were assessed in a field study using the Domain Specific Risk Taking scale and the Big Five Inventory scale. Assessors rated the risks and benefits for a mock “clinical dossier” specific to their area of expertise, and ordinal regression models were used to assess the odds of risk attitude or personality traits in predicting either the benefit or the risk ratings. **Results:** An increase in the “conscientiousness” score predicted an increase in the perception of the drug’s benefit, and male assessors gave higher scores for the drug’s benefit ratings than did

female assessors. Extraverted assessors saw fewer risks, and assessors with a perceived neutral-averse or aversive risk profile saw greater risks. **Conclusions:** Medical assessors perceive the benefits and risks of medicines via a complex interplay of the medical situation, their personality traits and even their gender. Further research in this area is needed to determine how these potential biases are managed within the regulatory setting.

**Keywords:** benefit-risk, heuristics, individual characteristics, risk attitude, risk perception.

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## Introduction

Medicinal products in Europe are regulated within a complex organizational structure encompassing more than 40 national competent authorities (NCAs) and relying on the expertise of 4500 experts or medical assessors throughout the European Union [1]. A substantial part of the assessment is under the responsibility of the medical assessors who work individually, or within groups, in the NCAs to evaluate the benefits and risks of medicinal drugs. In the field of risk research, there are several well-established findings that may be relevant to decision making for the regulation of medicines: 1) that benefit perception is the inverse of risk perception; 2) that the personality taxonomy from the Big Five Inventory (BFI) may intersect with risk attitudes and explain differences in risk taking; and 3) that risk attitudes (risk seeking, risk neutral, risk averse) are important descriptors for the shape of a decision-maker’s utility function underlying his or her choices [2–4]. A full discussion of each of the above-mentioned findings is beyond the scope of this article; however, a brief

summary of the literature and references to more detailed publications are provided below.

Alhakami and Slovic have observed that laypersons have a negative correlation between benefits and risks in that an activity or technology judged high in benefit is judged low in risk and vice versa [5]. An inverse relationship between benefit and risk perception implies the use of a heuristic, a subconscious rule of thumb that simplifies decision making by considering only a subset of the available information when arriving at a decision. The work of Gigerenzer and Brighton [6] and others [7,8] support the view of heuristics as an efficient means for managing uncertainty because it minimizes the need for complex computations when assessing situations and in many cases allows one to arrive at a similar level of accuracy as logic-laden decisions. There may, however, be instances when the application of a rule of thumb or a heuristic such as benefit-high/risk-low may be inappropriate given that medicines can have both increased benefits and increased risks. Evidence of the use of such a heuristic among assessors could indicate the introduction of

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biases in the decision making for medicinal drugs. It is therefore of interest to determine whether a benefit/risk heuristic, such as found among laypersons, is also used by assessors of medicinal drugs. Personality traits are known indicators of risk taking. Persons with higher levels of the traits extraversion and openness to experience tend to increase risk taking whereas persons with higher levels of the traits conscientiousness, neuroticism, and agreeableness decrease risk taking [8,9]. Personality traits are considered to be very relevant for optimizing organizational performance because they have been found to predict creativity and generation of superior ideas when an ‘optimal’ balance of personality traits is achieved within working teams [10]. The concept of risk attitudes (risk seeking, risk neutral/tolerant, and risk averse), when translated into the drug regulatory context, could imply that an assessor who is risk averse may be willing to give up the benefit a drug could provide to avoid the uncertainty regarding long-term adverse effects, whereas a risk-seeking assessor may be willing to accept some risks to avoid the sure loss of the drug not reaching the market. A risk-neutral/tolerant assessor may be seen as having an impartial view with a willingness to accept some degree of risk in every situation [2,11]. The risk attitude most often assigned to medical regulators is one of risk aversion [12,13]; however, there is no concrete evidence that medical regulators are uniformly risk averse. Despite its appeal, the term “risk attitude” as a stable individual trait (e.g., a person who exhibits a risk-averse utility function *does not like to take risks*) has had limited empirical support [4,14,15]. Works from Weber et al. [16] and others [14] have shown that individuals are not stable in their attitudes toward risk and may shift from being risk neutral to risk seeking depending on the domain (e.g., health vs. finance). Weber et al.’s [16] research, however, has also shown that an individual’s perception of the riskiness of a situation may be the lever that shifts risk attitude from averse to seeking; therefore, identification of a stable perception, if such exists, may be of great value in understanding individual or group decisions under situations of risk.

The research on benefit/risk heuristics, personality traits, and risk attitudes has been predominantly carried out among laypersons; experts have rarely been included in these studies primarily because of the assumption that given their expertise they consider only objective data when making judgments of risk and are not influenced by other factors [17,18]. There is growing evidence to contradict this view, and the authors direct readers to the work of Sjöberg [19] and others [20–22]. In 2009, the European Medicines Agency (EMA), the central body for regulating medicines in Europe, launched the EMA Benefit-Risk Methodology Project to assess the applicability of decision support tools within the regulatory environment [23–25]. Medical assessors in five European countries participated in field tests of methods aimed at improving the transparency of decision making [26,27]. One case study, not originally planned at the onset of the project, was the market authorization of the H1N1 (swine flu) vaccine. At the time, there was a genuine public health concern regarding the global impact of an impending contagious and sometimes fatal disease, and a decision regarding the market authorization of the vaccine was urgently needed. This, coupled with the lack of data on the efficacy and safety of the vaccine, created a highly charged environment. Consistent with the objectives of the EMA Benefit-Risk project, senior administrators at the EMA undertook to participate in a multicriteria decision analysis workshop (external to the normal decision-making process) to clarify their individual attitudes toward the benefits and risks of early or late approval of the vaccine. The result was a decision model that increased transparency of the assumptions regarding the number of expected fatalities if the decision was advanced or postponed. Although the final decision regarding the market authorization of the swine flu vaccine was not taken during this process, the use

of this methodology aided in defusing the tensions surrounding the decision by highlighting differences in risk attitudes among the participants and facilitating a more structured discussion of the implications to approve or not approve the vaccine [28].

Not all regulatory decisions are as charged as that of the swine flu vaccine, that is, a heightened emotional situation due to the potential for global fatalities with limited available data and short time period within which to consider the decision. This is not the only situation in which it may be appropriate to apply tools that support the regulatory process and remove the potential for the introduction of biases in the decision making. If medical assessors, like laypersons, are influenced by factors external to the scientific data even when working within their area of expertise, then tools such as multicriteria decision analysis or other structured approaches to decision making should be used to support their work.

In this study, we aimed to examine the risks and benefits of medicinal drugs as perceived by expert regulators and to assess the influence of personality traits and risk attitudes on their perceptions. Using Weber’s risk attitudes across domains as a measure of stable risk attitudes, our hypothesis is that assessors use the “benefit perception is the inverse of risk perception” heuristic and that personality traits and risk attitudes that indicate a propensity for greater risk taking among laypersons will also be found to indicate greater risk taking among assessors. Therefore, the objectives of this study were to 1) describe the distribution of risk attitudes among medical assessors, 2) measure their personality traits and cross-domain risk attitudes, 3) measure the correlation between benefit ratings and risk ratings of a medicinal product, and 4) predict the benefit and risk ratings of a medicinal product using the measured personality traits and risk attitudes.

## Methods

The study was implemented as a Web-based questionnaire and launched between June 2010 and October 2010. Medical assessors from nine European NCAs were identified by their agency and invited to participate. Demographic data were collected covering sex, country, age, education level, years in regulatory role, clinical area of cardiology, central nervous system, and oncology (clinical efficacy, clinical safety, nonclinical), and therapeutic area of expertise: central nervous system, cardiovascular, and oncology. Data were collected in three phases, with each phase lasting approximately 6 weeks: Phase 1: Demographic data, Domain Specific Risk Taking (DOSPERT) scale [29]; Phase 2: Drug Case Study using a mock “clinical dossier”; and Phase 3: The Big Five Jackson Inventory personality test [30].

### DOSPERT Scale

A number of scales have been developed to capture risk attitudes or behavior, but the DOSPERT scale was found to be the most appropriate for the aims of this study because it captures attitudes toward risk taking within several domains (social, financial, health/safety, recreational, and ethical) that encompass general life situations. In addition, the DOSPERT scale captures not only the attitude toward several types of activities within domains, but also the measurement of an individual’s perception of the riskiness and benefits of that activity.

The description of the DOSPERT scale provided by the authors is as follows: The risk-taking responses of the 30-item version of the DOSPERT scale evaluate behavioral intentions—or the likelihood with which respondents might engage in risky activities—originating from five domains of life (i.e., social, financial, health/safety, recreational, and ethical), using a seven-point rating scale,

ranging from 1 (*Extremely Unlikely*) to 7 (*Extremely Likely*). Sample items include “Disagreeing with an authority figure on a major issue” (Social), “Investing 10% of your annual income in a new business venture” (Financial), “Engaging in unprotected sex” (Health/Safety), “Taking a weekend sky-diving class” (Recreational), and “Having an affair with a married man/woman” (Ethical). The *risk perception* and the *benefit perception* scales pose the same questions as found in the risk taking scale, but here the aim is to evaluate the respondents’ assessment of the riskiness or the benefits of each activity, using a seven-point rating scale, ranging from 1 (*Not at all risky*) to 7 (*Extremely Risky*) (17) and 1 (*Not at all beneficial*) to 7 (*Extremely Beneficial*). Only the risk taking and risk perception scales of the DOSPERT scale were included in the present study. The addition of the benefit perception scale was felt to be too burdensome for the assessors given the length of the questionnaire. In addition, the benefit perception scale and the risk taking scale of the DOSPERT scale may be highly correlated because willingness to engage in an activity may be dependent on the benefit one perceives for that activity. The scores of the risk taking scale were added across all items of a given domain subscale to obtain risk-taking scores. Higher scores suggest a propensity for greater risk taking in that domain. Similarly, for the risk perception scale, item ratings are added across all items of the domain subscale to obtain risk perception scores and higher scores indicate a greater perception of risk.

Risk attitudes for both the risk taking and risk perception scales are presented as previously reported by Weber and Milliman [31] by domain and across the domains. The authors believe that both presentations are justified in that Weber and Milliman have proposed that a given risk attitude may be reflected within a specific domain but the measurement across all domains may reflect the general risk attitude (GRA) of a person irrespective of domain. Within each domain, respondent scores for both the risk taking and risk perception scales were categorized as risk seeking, risk neutral, and risk averse. Assessors whose subscale score was 1SD above or below the mean were categorized as risk seeking or risk averse, respectively; otherwise, they were categorized as risk neutral. For the analyses across domains, two new descriptors were used to categorize risk attitudes, reflecting the risk taking scale and the risk perception scale: GRA and perceived risk attitude (PRA). For both the GRA and PRA scales, the risk attitude of each assessor was classified as seeking, seeking/neutral, neutral, neutral/averse, averse, or mixed depending on her or his risk attitude found previously within each of the domains. An assessor’s GRA was categorized as seeking if he or she was identified as risk seeking for all five domains on the risk taking scale. If the assessor was classified as seeking for up to three domains and then neutral for the remaining, he or she was categorized as seeking/neutral. Similarly, for the PRA scale, an assessor was categorized as perceived neutral if he or she was neutral for all five domains on the risk perception scale. In cases where an assessors moved from risk seeking to neutral, they were categorized as perceived seeking/neutral. The “mixed” category identifies those who had no discernible pattern in their risk attitudes; for example, for one domain they were seeking, for another domain averse, and for another domain neutral.

Descriptive statistics of the risk taking and risk perception scores are presented and the correlation between the mean risk taking and mean risk perception scores by domain were assessed. Statistically significant Spearman correlation coefficients were set a priori at less than 0.05.

### Big Five Inventory

Five domains of personality (extraversion, openness, neuroticism, conscientiousness, and agreeableness) have been consistently identified using various instruments over several decades

and across many cultures and is therefore a highly regarded taxonomy [32–34]. The Big Five Inventory scale used in this area of research is a self-reported 44-item questionnaire to which respondents are asked to indicate whether they strongly disagree, disagree, are neutral, agree, or strongly agree. An example of the description for openness would include “I have a rich vocabulary,” “I have a vivid imagination,” “I have excellent ideas” [30,35]. Mean scores and SDs for each trait are presented. Higher scores within the domains indicate a greater propensity for the personality trait being measured.

### Mock Clinical Dossiers

In the second phase of the study, assessors were given a mock “dossier” specific to their therapeutic area of expertise (cardiology, central nervous system, and oncology). The cardiology product was indicated for the treatment of atrial fibrillation; the central nervous system product was indicated for the treatment of neuropathic pain; and the oncology product was indicated for the treatment of non-small cell lung cancer. Data for the mock dossiers were adapted from the original product dossiers, day 80 assessment reports, and European Public Assessment Reports [36]. The result was a shortened version of a real dossier, with product-identifying data (e.g., drug name, manufacturer, and dates) removed or substituted. The assessors were asked to review the dossier and to give their perceptions by rating the medicinal product on two dimensions, risk and benefit. Both ratings used a Likert-like scale ranging from 1 to 7; for the risk dimension, the question was “How risky is this product?” Possible risk ratings ranged from 1 (*not at all risky*) to 7 (*extremely risky*). For the benefit dimension, the question was “How beneficial is this product?” Benefit ratings ranged from 1 (*not at all beneficial*) to 7 (*extremely beneficial*). The assessors were constrained not to consult with their colleagues because the aim of the study was to collect their individual benefit and risk perceptions of the medicinal products.

### Model Building

Ordinal regression models were used to evaluate the relationship between the rating of benefits and risks for a medicinal product (one product in each of the disease areas previously mentioned), BFI traits, and risk attitudes from the DOSPERT scale. Ordinal regression models are an extension of the general linear model to ordinal categorical data. This method is very useful in social sciences in which data are often captured as ordinal variables, limiting the usefulness of linear models that require interval variables. The ordinal model tests the probability of any category of the independent variables being in a particular category of the dependent variable or lower, compared with a reference group. Negative parameter estimates indicate lower scores for the benefit or risk ratings, whereas positive estimates indicate choosing higher scores. For both the GRA and the PRA, the category with the largest proportion of assessors was the seeking-neutral category and this was therefore chosen as the reference category.

Because of limited published data on personality traits and experts, several models were evaluated responding to our research objectives. To determine which of the BFI dimensions was most relevant to this analysis, bivariate analyses were conducted using a backwards stepwise regression selection procedure between the benefit ratings and the five dimensions of the BFI. please insert next sentence ‘A similar procedure was conducted for the risk ratings and the BFI dimensions. At each iteration of the model, the BFI dimension with the lowest nonstatistically significant Wald statistic was dropped. Assessors reviewed dossiers relevant to their area of expertise; therefore, a variable, denoting the three

**Table 1 – Demographic characteristics.**

Variable	Characteristic	Frequency	
Sex	Male	38	
	Female	37	
Age (y)	Between 20 and 29	1	
	Between 30 and 39	22	
	Between 40 and 49	30	
	Between 50 and 59	18	
	>60	3	
Professional qualifications	MD	27	
	MD/PhD	11	
	PhD	19	
	PhD/Pharm	3	
	Pharmacist	10	
	Other	5	
Role in NCA	CHMP member	6	
	Internal assessor	57	
	External assessor	9	
	Other	3	
Years of regulatory experience by country		<5 y	5+ y
	France	2	8
	Spain	4	3
	The Netherlands	8	3
	United Kingdom	4	6
	Germany	3	7
	Austria	9	1
	Italy	10	0
	Ireland	0	3
	Portugal	1	3

CHMP, Committee for Medicinal Purposes for Human Use; NCA, National Competent Authority.

medicinal products in the mock dossiers, was included during model building. In previous research, sex has been found to be predictive of risk perception and so was also included in the models. Previous work in this area has shown a correlation between willingness to engage in risky activities depending on how risky the activity is perceived; therefore, separate models evaluating the GRA and the PRA were constructed.

Following the bivariate analysis described above, separate models were built for benefit ratings and risk ratings. Benefit ratings were regressed on the BFI personality traits identified from the bivariate analysis along with the GRA categories, sex, and therapeutic area. A forward and backwards stepwise regression selection method was used to determine the final model with the best model fit [37]. Variables with nonstatistically significant estimates ( $>0.05$ ) were removed at each iteration. The evaluation of the benefit ratings and the PRA categories, sex, and therapeutic area followed the same model-building approach as above. This process was replicated for building the models for the risk ratings. All parameter estimates

with statistically significant results at the less than 0.05 level are reported along with data for model fit. The authors are aware that the use of stepwise regression methods has several limitations and that there are alternatives to this approach (e.g., testing the final model in an independent sample), but given the peculiarity of the study sample, that is, the limited availability of European medical assessors, the uniqueness of the sample population, and the number of variables included for testing (DOSPERT, Big Five taxonomy), the chosen approach appeared to be the most pragmatic. All statistical analyses were conducted using SPSS 18.

## Results

### Demographic Characteristics

Of the 80 assessors enrolled in the study, 75 (94%) responded in phase 1, while 59 (73%) assessors completed phases 2 and 3. No

**Table 2 – Descriptive statistics of DOSPERT scale—Risk taking by domain.**

Domain	N	Mean $\pm$ SD	Skewness		Kurtosis	
			Statistic	SE	Statistic	SE
Social mean score	75	5.3707 $\pm$ .78685	−0.392	.277	−0.251	.548
Financial mean score	75	2.3344 $\pm$ 1.13292	1.119	.277	1.612	.548
Health safety mean score	75	2.4200 $\pm$ 0.96771	1.010	.277	0.866	.548
Recreational mean score	75	2.9542 $\pm$ 1.16136	0.423	.277	−0.419	.548
Ethical mean score	75	1.8813 $\pm$ 0.76816	1.536	.277	3.594	.548
Valid N (listwise)	75					

DOSPERT, Domain Specific Risk Taking; SE, standard error.



**Table 3 – DOSPERT scale—Risk taking and risk perception within the five domains.**

Domain	Risk seeking		Risk neutral/tolerant		Risk averse	
Risk taking	Row N = 75	%	Row N = 75	%	Row N = 75	%
Social	19	25.3	46	61.3	10	13.3
Financial	14	18.7	47	62.7	14	18.7
Health/safety	9	12.0	57	71.0	9	12.0
Recreational	12	16.0	51	68.0	12	16.0
Ethical	14	18.7	53	70.7	8	10.7
Risk perception	Row N = 75	%	Row N=75	%	Row N=75	%
Social	9	12.0	53	70.7	13	17.3
Financial	13	17.3	48	64.0	14	18.7
Health/safety	14	18.7	50	66.7	11	14.7
Recreational	13	17.3	46	61.3	16	21.3
Ethical	13	17.3	49	65.3	13	17.3

DOSPERT, Domain Specific Risk Taking.

difference was found for age, sex, role in the agency, regulatory experience, or therapeutic area expertise between dropouts from phase 1 and those who continued on to phases 2 and 3.

As presented in Table 1, the group was equally balanced by sex; 31% were between 20 and 39 years old. Many assessors had multiple educational degrees; 51% of the assessors were medically qualified, followed by PhD (29%) and pharmacists (13%). Assessors within the NCAs generally focus on single area of expertise. In our sample, most of the assessors were experts in assessing clinical efficacy (63.8%). Assessors with less than 5 years of experience comprised most of the group (55%).

### Risk Attitudes among Assessors

The mean scores for the DOSPERT scales (risk taking and risk perceptions) for the five domains (social, financial, health/safety, recreational, and ethical) are given in Table 2. When the domain subscale scores for both risk taking and risk perception scales were categorized by domain, assessors were predominantly risk neutral/tolerant, with the remaining assessors evenly distributed among the other categories (Table 3). When the risk taking scale was evaluated across the domains as presented in Table 4, 2.5% of the assessors were risk seeking for all domains, no assessor was risk averse for all domains, and 15% of the assessors were neutral/tolerant in their GRA. Similarly, for the risk perception scale, 2.5% of the assessors were categorized as being “perceived risk seeking” for all domains and 2.5% were “perceived risk averse” for all domains, while 17.5% of the assessors were perceived risk neutral/tolerant.

Earlier research has shown a relationship between willingness to engage in risky activities depending on how risky the activity is

perceived. We evaluated this relationship using a correlation analysis between risk taking in each domain and the corresponding risk perception of the activity. There was a statistically significant inverse relationship between mean risk-taking score and mean risk-perception score (Table 5) for all domains with the exception of the social domain. The correlation analysis shows that the riskier an activity is viewed by the assessors, the less likely they are to engage in it.

### Big Five Inventory

The scores for the BFI dimensions were normally distributed, with the following means and standard deviations: extraversion,  $3.3 \pm 0.738$ ; conscientiousness,  $4.1 \pm 0.627$ ; agreeableness,  $3.8 \pm 0.443$ ; neuroticism,  $2.5 \pm 0.704$ ; openness,  $3.9 \pm 0.461$ . The regression coefficient of the bivariate analysis for the BFI dimensions showed only conscientiousness (BFIC) to be predictive of the benefit rating (0.519;  $P = 0.027$ ); that is, more conscientious individuals saw more benefit. Extraversion (BFIE) was found to be predictive of risk rating ( $-0.406$ ;  $P = 0.047$ ), in that the more extraverted assessors saw less risks attached to the drug. All other BFI dimensions were nonsignificant and therefore excluded from further modeling.

### Distribution and Correlation of Benefit and Risk Ratings

For both the benefit and risk scales, the rating has a normal distribution, with most of the ratings in the middle of the 1 to 7 range. The ratings were reclassified from ordinal to interval variables for the purpose of the correlation analysis, and a

**Table 4 – DOSPERT scale—Risk attitudes across all domains.**

Risk attitude categories	General risk attitude (from the Risk Taking subscale)		Perceived risk attitude (from the Risk Perception subscale)	
	N = 75	%	N = 75	%
Seeking	2	2.5	2	2.5
Seeking neutral	26	32.5	28	35.0
Neutral	12	15.0	14	17.5
Neutral averse	24	30.0	25	31.2
Averse	0	0	2	2.5
Mixed	11	13.8	4	5.0

DOSPERT, Domain Specific Risk Taking.

**Table 5 – Correlation results between the DOSPERT Risk Taking and Risk Perception subscales.**

Domain	Spearman rho	Significance (0.05)
Social	–.149	.203
Financial	–.343*	.003*
Health/safety	–.357*	.002*
Recreational	–.470*	.000*
Ethical	–.350*	.002*
DOSPERT, Domain Specific Risk Taking.		
* Statistically significant <0.05.		

statistically significant inverse correlation between the benefit and risk ratings was found ( $-0.309$ ;  $P = 0.017$ ).

### Ordinal Regression for the Benefit Rating—GRA, PRA, and BFIC

It has been shown above that BFIC (conscientiousness) was predictive of the benefit ratings; the addition of the GRA categories did not improve the model and was therefore dropped. Sex differences have been found in many studies in risk taking, and men in general have been found to be more risk taking and to perceive fewer risks than do women [38,39]. Sex and therapeutic area were added to the model, but therapeutic area was not statistically significant and did not improve the model fit and was therefore removed. With only BFIC and sex in the model, the PRA categories were added but as with the GRA categories, this variable was not statistically significant. The final model was therefore BFIC (0.497;  $P = 0.036$ ) and sex (0.594;  $P = 0.041$ ), showing that controlling for sex, an increase in the score for conscientiousness increased the probability of giving higher benefit scores, and similarly controlling for BFIC, male assessors gave higher benefit scores than did female assessors (Table 6).

### Ordinal Regression for the Risk Rating—GRA, PRA, and BFIE

As above, the starting point for the model structure was the bivariate analysis with the risk ratings and BFIE (extraversion). Additional bivariate models for the GRA ( $\chi^2 = 1.267$ ;  $P = 0.867$ ), sex ( $\chi^2 = 0.206$ ;  $P = 0.650$ ), and therapeutic area were constructed, and all were shown to be nonpredictive of the risk ratings with the exception of the therapeutic area (Table 7). Using the model with therapeutic area as the basic model, the other predictor variables of interest were again added or dropped depending on whether an improvement in the model fit was observed. The BFIE and the PRA categories along with therapeutic area resulted in the most robust

model for predicting the risk ratings (Table 8). Assessors with higher scores for extraversion were more likely to give lower risk ratings. Compared with those in the perceived risk seeking-neutral category, the neutral-averse, aversive, and mixed categories were more likely to give higher risk ratings, controlling for therapeutic area.

## Discussion

To our knowledge, this is the first study to examine personality traits and risk attitudes within the pharmaceutical regulatory network in Europe. The study aims to examine relationship between risk perception and benefit perception among expert assessors, as measured by the benefit and risk rating of three medicinal products. One of our key findings is that, as for laypersons, benefits and risks are inversely correlated among medical assessors. We believe that this is indicative of a heuristic that may in some cases be veridical, that is, truly reflective of the assessment of the drug but may also lead assessors to negate true benefits when there are high risks and prevent a balanced assessment. This inverse relationship of benefits and risks although providing us with an important view of the mental model of experts in drug regulation should not serve as the sole explanation of the assessment process. We argue, on the basis of results of this study, that the mental models of assessors are far more complex than previously assumed and that assessors rely on a complex interplay of risk attitudes and personality traits as well as the perception of the clinical data when assessing medicinal drugs.

The results from the DOSPERT scale are useful in countering a pervasive view that regulators have a shared and stable “risk-averse” attitude [12,13,40]. Instead, we show that for the domains measured, assessors are predominantly risk neutral/tolerant and may even perceive fewer risks than did the sample of US undergraduates in the Weber et al. [16] study. With the exception of risk neutral attitude there was no evidence of assessors having a predominant risk attitude, across all domains; in line with previous research among laypersons, assessors change their risk attitude, for example, move from seeking to neutral, or neutral to aversive, depending on the domain. However, it may be that within the risk attitude categories we have defined using the across-domain classification, there may be a stable risk attitude measurable from the PRA scale but not from the GRA. Perhaps the GRA with its focus on behavioral intentions (*what is the likelihood of engaging in this activity?*) does not provide a measure of the perceived risks involved and therefore cannot be used to indicate risk propensity in areas outside those measured in the DOSPERT scale. Results of the PRA scale with its focus on risks (*how risky is this activity?*) across

**Table 6 – Ordinal regression results for the benefit ratings—BFIC and sex (N = 59).**

Location	Estimate	SE	Wald	df	Significance
BFIC	.497	.237	4.384	1	0.036
Male	.594	.290	4.191	1	0.041
Female	0	–	–	0	–
Model	–2 log likelihood		$\chi^2$	df	Significance
Intercept Only	156.377		8.825	2	0.012
Final	147.553				
Goodness of fit			$\chi^2$	df	Significance
Pearson			137.060	178	0.990
Deviance			118.309	178	1.000
BFIC, Big Five Inventory conscientiousness; SE, standard error.					

**Table 7 – Ordinal regression results for the risk ratings—Therapeutic area (N = 59).**

Location	Estimate	SE	Wald	df	Significance
Cardiovascular	−.820	.364	5.079	1	0.024
CNS	−.728	.338	4.636	1	0.031
Oncology	0	–	–	0	–
Model	−2 log likelihood		$\chi^2$	df	Significance
Intercept only	45.095				
Final	38.517		6.579	2	0.037
Goodness of fit			$\chi^2$	df	Significance
Pearson			4.757	8	0.783
Deviance			5.181	8	0.738
CNS, central nervous system; SE, standard error.					

CNS, central nervous system; SE, standard error.

domains, however, can be used as an indicator for a stable personality trait; that is, assessors who can be categorized as belonging to the seeking-neutral group may be less conservative than those in the neutral-averse, averse, and mixed groups and may view other life domains such as assessment of pharmaceutical drugs through this lens.

In the regression analysis, the benefits and risk scores are explained by individual characteristics, namely, personality traits and PRA. We have shown in previous work that medical assessors' risk perception of the three medicinal drugs is specific to the situation under review: the type of product, the safety and ethical concerns, the number of patients potentially impacted by the adverse effects of the medicinal product, and individual characteristics such as years of experience as an assessor and sex [20]. It now appears that personality traits also influence the perception of benefits and risks. It is surprising that conscientiousness and extraversion were the only personality traits from the BFI to be predictive of the benefit and the risk ratings, respectively, because the other BFI personality traits (openness, neuroticism, and agreeableness) have also been found to be predictive of increasing or

depressing risk taking in other situations [9]. Conscientiousness is described as the state of being thorough, careful, or vigilant; it implies a desire to do a task well and has been found to be influential of job performance [41,42]. Therefore, highly conscientious medical assessors may be sensitive to the promise of the benefits of medicinal products and may place great value on these aspects when reviewing a medical dossier. Sex was considered a potential confounder for the relationship between BFIC and the benefit ratings, and the additive model constructed shows that indeed both variables contribute to explain the variance in the benefit ratings. The implication of these results, when the benefit-risk assessment of medicinal drugs is carried out in teams as it is in Europe, is that careful thought should be given to the composition of personality traits and risk attitudes to minimize the negative effects on team processes of certain personality traits and maximize the positive effects of others similar to the consideration given to the impact of cognitive styles on task execution [10,43].

The authors believe the results show that there is a human dimension that influences the perceptions of assessors, which is not negated simply by their expertise. Assessors are susceptible

**Table 8 – Ordinal regression results for the risk ratings—BFIE, therapeutic area, and perceived risk attitudes (N = 59).**

Variables	Estimate	SE	Wald	df	Significance
Location					
BFIE	−0.636	0.230	7.634	1	0.006
Cardiovascular	−1.246	0.435	8.210	1	0.004
CNS	−0.684	0.371	3.410	1	0.065
Oncology	0	–	–	0	–
Perceived risk attitudes					
Seeking	0.304	1.126	0.073	1	0.788
Neutral	0.049	0.433	0.013	1	0.910
Neutral-averse	0.761	0.358	4.523	1	0.033
Averse	2.738	1.225	4.994	1	0.025
Mixed	2.728	0.981	7.731	1	0.005
Seeking-neutral	0	0	0		0
Model	−2 log likelihood		$\chi^2$	df	Significance
Intercept only	177.225				
Final	152.865		24.360	8	0.002
Goodness of fit			$\chi^2$	df	Significance
Pearson			241.156	252	0.677
Deviance			148.706	252	1.000

BFIE, Big Five Inventory extraversion; CNS, central nervous system; SE, standard error.



to the same failings as laypersons, and this should be acknowledged within the regulatory process. The EMA within the Benefit-Risk Methodology project has taken steps in this direction, and the swine flu case study provides one example of an “ideal” decision-making environment in which “hidden” or subconscious assumptions are made transparent. This does not mean that the decision resulting from such a process will be considered “right” but that every opportunity has been taken to increase the objectivity of the assessment and decrease the subjectivity inherent to any human decision-making process.

This study, although providing important additional knowledge regarding benefit and risk perception of medicinal products and the interaction with individual and personality traits, has several limitations. The lack of predictive power of the GRA scale may be due to the specific risk-taking activity questions found in the DOSPERT scale, which may not fit the regulatory domain. In addition, the long duration of the study necessary for gathering data in this natural setting resulted in a 77% response rate by the final phase during which the BFI scale measurements were taken. The resulting sample of assessors within our study appears to be small; however, the authors hasten to point out that the seemingly small number of medical assessors is inherent in the design of the study because we wished to focus on assessors with expertise in specific disease areas. Nonetheless, future research could aim to enroll a larger sample of assessors to test the validity of the results and also to explore the impact of individual personality traits on group decision making within the national agencies. Despite the above-mentioned limitations, our results remain useful for generating future hypotheses and are among the few available on expert medical assessors who are, understandably, not readily accessible for behavioral studies because of the confidential nature of their work and their heavy work commitments.

## Conclusions

There is a pervasive belief that decision-making bodies, such as the European regulatory network, by virtue of their organizational structure allows for alternative perspectives to be rationally considered until the optimal decision is reached [44], relying on a hierarchical bottom-up flow of expert advice and consultation. There is, however, evidence to contradict this view; that is, real-life organizational decision making is prone to both cognitive and organizational limitations and problems of ambiguity, uncertainty, and conflict. In addition, individual risk attitudes and perceptions may negatively impact the elucidation and consideration of the alternatives [44]. Our first contribution to the extensive body of work on risk perception is the observation that the perception of benefits that accompany medicines is as equally complex as that of risks. Similar to laypersons, experts view benefits as negatively related to risks. We encourage the investigation of benefit perception alongside that of risk perception. A second contribution is that experts perceive the risks of a hazard via a set of situational and individual characteristics and therefore the decision of what is risky is a complex interplay of the situation, their level of expertise, their perception of the risks involved, and even their sex [4,18,45–47]. The knowledge that individual characteristics such as personality traits may be influential in the way assessors perform their job is not surprising because like laypersons they are prone to biases and reliance on heuristics; however, it is important to provide empirical evidence of what maybe important influences in the decision-making process and to challenge those responsible to create diverse decision-making teams in which individual factors are appropriately balanced. The authors recommend that medical assessors within the national agencies participate in an evaluation that assesses their GRAs and their personality traits. Workshops, similar to those conducted by the EMA Benefit-Risk Methodology Project to demonstrate the

application of decision support tools, could be organized within the NCAs. The aim of the workshop should be to educate medical assessors on the evidence of risk perception, risk attitude, and personality trait literature; to demonstrate the impact of their personality traits on decision making; and to show how decision support tools can aid the transparency and minimize the impact of these traits.

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## REFERENCES

- [1] European Expert List. London: European Medicines Agency. Available from: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/landing/experts.jsp&mid=WCOb01ac050843244a](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/experts.jsp&mid=WCOb01ac050843244a). [Accessed March 22, 2013].
- [2] Kahneman D, Tversky A. On the psychology of prediction. *Psychol Rev* 1973;80:237–51.
- [3] Hillison D, Murray-Webster R. Understanding and Managing Risk Attitude. Hants. England: Gower Publishing, 2007.
- [4] Slovic P. Assessment of risk-taking behaviour. *Psychol Bull* 1964;61:330–3.
- [5] Alhakami A, Slovic P. A psychological study of the inverse relationship between perceived risk and perceived benefit. *Risk Analysis* 1994;14:1085–96.
- [6] Gigerenzer G, Brighton H. Homo heuristicus: why biased minds make better inferences. *Top Cog Sci* 2009;1:107–43.
- [7] Marewski JN, Gigerenzer G. Heuristic decision making in medicine. *Dialogues Clin Neurosci* 2012;14:77–89.
- [8] Nicholson N, Soane E, Fenton-O'Creevy M, Willman P. Personality and domain-specific risk taking. *J Risk Res* 2005;8:157–76.
- [9] Deck C, Lee J, Reyes J, Rosen C. Measuring risk attitudes controlling for personality traits 2009. Available from: [http://www.econ.canterbury.ac.nz/research/pdf/Paper\\_Deck.pdf](http://www.econ.canterbury.ac.nz/research/pdf/Paper_Deck.pdf) [Accessed December 10, 2014].
- [10] Buchanan LB. The Impact of Big Five Personality Characteristics on Group Cohesion and Creative Task Performance. Blacksburg, VI: Virginian Polytechnic Institute, 1998.
- [11] Kahneman D, Tversky A. Judgment under uncertainty. *Science* 1974;185:1124–31.
- [12] Gilland T. The politics of changing the ‘Risk Averse’ mentality in western society—a case study of the GM debate in Britain and Europe. In: The American Enterprise Institute conferences “Biotechnology, the Media and Public Policy. Washington, DC, 2003.
- [13] Gill T. No Fear: Growing Up in a Risk-Averse Society. London, UK: Calouste Gulbenkian Foundation, 2007.
- [14] Schoemaker PJH. Determinants of risk-taking: behavioral and economic views. *J Risk Uncert* 1993;6:49–73.
- [15] Keller LR. An empirical investigation of relative risk aversion. *IEEE Trans Systems Man Cybernet* 1985;15:475–82.
- [16] Weber EU, Blais AR, Betz N. A domain-specific risk-attitude scale: measuring risk perceptions and risk behaviors. *J Behav Decis Making* 2002;15:263–90.
- [17] Flynn J, Slovic P, Mertz CK. Decidedly different: expert and public views of risks from a radioactive waste repository. *Risk Analysis* 1993;13:643–8.
- [18] Slovic P. Perception of risk. *Science* 1987;236:280–5.
- [19] Sjöberg L. The allegedly simple structure of experts’ risk perception: an urban legend in risk research. *Science Technol Hum Values* 2002;27:443–59.
- [20] Beyer A, Fasolo B, Phillips L, et al. Risk perception of prescription drugs: results of a survey among experts in the European regulatory network. *Med Decis Making* 2013;33:579–92.

- [21] Rowe G, Wright G. Differences in experts and lay judgements of risk: myth or reality? *Risk Analysis* 2001;21:341–56.
- [22] Otway H. Public wisdom, expert fallibility: toward a contextual theory of risk. In: Krinsky S, Golding D, eds., *Social Theories of Risk*. Westport, CT: Praeger-Greenwood, 1992.
- [23] Phillips L. Applicability of Current Tools and Processes for Regulatory Benefit-Risk Assessment (Adopted September 2010) (Work Package 2). London, UK: European Medicines Agency, Safety and Efficacy of Medicines, 2010.
- [24] Phillips L, Fasolo B, Zafiroopoulos N, Beyer A. Is quantitative benefit-risk modelling of drugs desirable or possible? *Drug Discov Today Technol* 2011;8:e3–10.
- [25] Phillips L. Description of the Current Practice of Benefit-Risk Assessment for Centralized Procedure Products in the EU Regulatory Network (Adopted December 2009). London, UK: European Medicines Agency, Safety and Efficacy of Medicines, 2009.
- [26] European Medicines Agency. Benefit-Risk Methodology Project. European Medicines Agency, 2009.
- [27] European Medicines Agency. Field-Testing the Most Appropriate Models in Five European Medicine Regulatory Agencies (Work Package 3). European Medicines Agency. Medicines SaEo 2011.
- [28] Phillips L, Fasolo B, Zafiroopoulos N, et al. Modeling the risk-benefit impact of H1N1 influenza vaccines. *Eur J Public Health* 2013;23:674–8.
- [29] Blais AR, Weber E. A Domain-Specific Risk-Taking (DOSPERT) scale for adult populations. *Judg Decis Making* 2006;1:33–47.
- [30] John OP, Naumann LP, Soto CJ. Paradigm shift to the integrative big-five trait taxonomy: history, measurement, and conceptual issues. In: John OP, Robins RW, Pervin LA, eds., *Handbook of Personality: Theory and Research*. (3rd ed.) New York, NY: Guilford Press, 2008.
- [31] Weber EU, Milliman RA. Perceived risk attitudes: relating risk perception to risky choice. *Manag Sci* 1997;43:123–44.
- [32] McCrae RR, Costa PT. Validation of the five-factor model of personality across instruments and observers. *J Person Soc Psychol* 1987;52:81–90.
- [33] McCrae RR, Costa PT. Personality trait structure as a human universal. *Am Psychol* 1997;52:509–16.
- [34] McCrae RR, Terracciano A. Personality Profiles of Cultures Project. Universal features of personality traits from the observer's perspective: data from 50 different cultures. *J Person Soc Psychol* 2005;88:547–61.
- [35] John OP. The “Big Five” factor taxonomy: dimensions of personality in the natural language and in questionnaires. In: Pervin L, ed. *Handbook of Personality: Theory and Research*. New York: Guilford Press, 1990.
- [36] Procedures for Marketing Authorization. London: European Medicines Agency, 2006.
- [37] Hocking RR. The analysis and selection of variables in linear regression. *Biometrics* 1976;32:1–49.
- [38] Byrnes JP, Miller DC, Schafer WD. Gender differences in risk taking: a meta-analysis. *Psychol Bull* 1999;125:367–83.
- [39] Harris CR, Jenkins M. Gender differences in risk assessment: why do women take fewer risks than men? *Judg Decis Mak* 2006;1: 48–63.
- [40] Vogel D. The New Politics of Risk Regulation in Europe. UK: The London School of Economics and Political Science, 2001.
- [41] Salgado JF. The Five Factor Model of personality and job performance in the European Community. *J Appl Psychol* 1997;82:30–43.
- [42] Barrick MR, Mount K. The big five personality dimensions and job performance. *Personnel Psychol* 1991;44:1–26.
- [43] Aggarwal I, Woolley-Williams A. Do you see what I see? The effect of members' cognitive styles on team processes and errors in task execution. *Organ Behav Human Decis Process* 2012;122:92–9.
- [44] March JG. How decisions happen in organizations. *Human-Comput Interact* 1991;6:95–117.
- [45] Slovic P, Kraus NN, Lappe H, et al. Risk perception of prescription products: report on a survey in Sweden. *Pharmaceut Med* 1989;4: 43–65.
- [46] Slovic P, Kraus N, Lappe H, Major M. Risk perception of prescription products: report on a survey in Canada. *Can J Public Health* 1991;82 (Suppl):S15–20.
- [47] Slovic P, Peters E, Grana J, et al. Risk perception of prescription products: results of a national survey. *Drug Inf J* 2007;41:81–100.